

What is claimed is:

1 1. A method for increasing the proliferation of
2 thymocytes in a non-human animal comprising altering an endogenous
3 gene encoding p27^{Kip1} in a somatic cell of the animal to cause a
4 functional deficiency of cyclin-dependent kinase inhibitor function
5 of p27^{Kip1}, thereby increasing the proliferation of thymocytes in the
6 animal.

1 2. The method of claim 1, wherein the cell is a
2 thymocyte or bone marrow cell.

1 3. The method of claim 1, wherein the animal is a
2 rodent, pig, sheep, frog, or bovine.

1 4. The method of claim 1, wherein the gene encoding
2 p27^{Kip1} is altered by insertion of a positively selectable marker,
3 mutation of the gene encoding p27^{Kip1}, or deletion of the gene
4 encoding p27^{Kip1}.

1 5. The method of claim 4, wherein the gene encoding
2 p27^{Kip1} is altered by insertion of a positively selectable marker
3 into the gene.

1 6. The method of claim 5, wherein the positively
2 selectable marker encodes neomycin resistance, thymidine kinase,
3 adenine phosphoribosyl transferase, hypoxanthine-guanine
4 phosphoribosyl transferase or dihydrofolate reductase.

1 7. The method of claim 6, wherein the positively
2 selectable marker encodes neomycin resistance.

1 8. The method of claim 1, further comprising:
2 introducing a plasmid into the cell, wherein the plasmid
3 comprises the gene encoding p27^{Kip1} altered by insertion of a
4 positively selectable marker.

1 9. The method of claim 8, wherein the plasmid further
2 comprises a negatively selectable marker adjacent the altered gene
3 encoding p27^{Kip1}, whereby the distance between the negatively
4 selectable marker and the altered gene encoding p27^{Kip1} is sufficient
5 to allow homologous recombination between the altered gene encoding
6 p27^{Kip1} and a gene encoding p27^{Kip1} in the cell.

1 10. The method of claim 9, wherein the negatively
2 selectable marker encodes thymidine kinase.

1 11. The method of claim 8, wherein the plasmid is
2 delivered to the cell by electroporation, microinjection or
3 transformation.